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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/716,293	MASSIA ET AL.	
	Examiner	Art Unit	
	Ronald T. Niebauer	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/19/07*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-101* is/are pending in the application.

4a) Of the above claim(s) *2-4,6 and 9-101* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,7 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/10/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I (claims 1-20,25-46,101) and the species of SEQ ID NO:124 in the reply filed on 10/3/06 and clarification of the species (3/12/07) and sequence identifier (8/10/07) is acknowledged.

Section 803.02 of the MPEP highlights the examination of claims that recite alternatives:

> On the other hand, should the examiner determine that the elected species is allowable, the examination of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. The prior art search, however, will not be extended unnecessarily to cover all nonelected species.

In the instant case, the elected species is SEQ ID NO:124 as recited in claim 8. SEQ ID NO:124 (CNAFKILVVITDGEK) was found to be free of the prior art. The closest art (Rieu 1994 as cited in IDS) recites a fragment of this peptide excluding the first cysteine residue (NAFKILVVITDGEK, peptide A7 of figure 6). However, Rieu does not expressly teach or motivate a cysteine residue as the first amino acid of the protein. Since no claim is drawn solely to SEQ ID NO:124 no claim is indicated as allowable. The examiner extended the search to another species of claim 8 and found art that rendered obvious the claim. The claims to nonelected species are held withdrawn from consideration. In the course of searching for the species of claim 8 other prior art (see 102 rejection) was uncovered and is cited herein.

Claims 2-4,6,9-101 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention/species, there being no allowable generic or

linking claim. Election was made **without** traverse in the reply filed on 10/3/06 and clarification of the species (3/12/07) and sequence identifier (8/10/07).

Claims 1,5,7-8 are under consideration.

Specification

Applicant is reminded of the following requirement:

In a continuation or divisional application (other than a continued prosecution application filed under 37 CFR 1.53(d)), the first sentence(s) of the specification or application data sheet (37 CFR 1.76) should include a reference to the prior application(s) from which benefit is sought. See 37 CFR 1.78. The following format is suggested: "This is a continuation (or divisional) of Application No._____, filed_____, now (abandoned, pending or U.S. Patent No._____)."

In the instant case applicant has identified the application as a continuation in part of a pending application (10/295,734). Application 10/295,734 is abandoned (not pending) and this status should be updated.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 recites that the bioconjugate is comprised of peptides selected from SEQ ID NO:1-202. However, SEQ ID NO:1, for example, is not a peptide. SEQ ID NO:1 is a nucleic acid sequence. A peptide is composed of amino acids, not nucleic acids.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1,5,7-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional

characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the claims are drawn to a bioconjugate comprising a hydrophilic polymer and a peptide (claim 1), a bioconjugate in which the peptide is from a particular class (claims 5,7) or of particular amino acid sequences (claim 8).

(1) Level of skill and knowledge in the art:

The level of skill in the art is high.

(2) Partial structure:

The bioconjugate is composed of a hydrophilic polymer and a peptide. Specific examples of peptides are revealed in claim 8 for example. However, the peptide as described in claims 1,5, and 7 is very broad. Claim 1 recites that the peptide is capable of binding to a ligand. The degree of binding is not specified. Nearly every peptide is capable of binding to a ligand. Therefore nearly any possible peptide could meet the limitation of claim 1b. However, the examples provided in the specification are from a very limited subset of peptides – integrin alpha or integrin beta subunit peptides. There are many more classes of proteins that could be used. For example, there are hundreds of G-protein coupled receptors that are capable of binding a ligand. Even within the integrin family there are many possible peptides. For example Liu et al. (US

5,340,800 cited below) disclose a variety of integrin peptides (specifically CD18 peptides see table 1 of Liu, column 11-12). Hence, there is substantial variability in the genus.

Regarding the polymer, the specification recites that the polymer could be for example a polysaccharide, a dextran, a PEG (page 6), or could even be a peptide. Hence, there is substantial variability in the genus. However, examples of specific bioconjugates combined with peptides are limited to Examples 1 and 3 in which the peptide CNAFKILVVITDGEK , CTVDLKFGIKNIEAV, or KCENGADFTKIIVLV were conjugated with dextran. No core sequence is taught for all of the possible polymers. As currently claimed the polymer could have saccharides, polyethylene, amino acids or combinations thereof as the repeating units.

Claim 1 is also drawn to one or more peptides, however specific examples of a bioconjugate with multiple peptides are not provided. It is noted that claim 8 provides written description for specific peptides but does not provide adequate written description for hydrophilic polymers.

Taken together, since there are a substantial variety of bioconjugates possible within the genus, the examples do not constitute a representative number of species and do not sufficiently describe the genus claimed (see Gostelli above). Of the many possible bioconjugates specific examples are only provided for 3 different peptides and one polymer.

(3) Physical and/or chemical properties and (4) Functional characteristics:

Claim 1 recites that the peptide is capable of binding to a ligand. The degree of binding is not specified. Nearly every peptide is capable of binding to a ligand. No specific core sequence is taught in claim 1,5,7 to identify which specific peptides are envisioned. There is no disclosure of

a correlation between function and structure. The bioconjugate comprises a hydrophilic polymer. No specific core sequence or functional groups of the polymer are recited in claims 1,5,7-8.

(5) Method of making the claimed invention:

The specification (specifically example 1) describes synthesis of SEQ ID NO:124.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 1 is/are broad and generic, with respect to all possible bioconjugates encompassed by the claims. Although the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the polypeptides beyond those polypeptides specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of polypeptides identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of polypeptides embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Faanes et al. (US 5,695,760).

Faanes teach a PEG (polyethylene glycol) derivative of a protein capable of binding to ICAM-1 (claim 1 for example). PEG is a hydrophilic polymer (compare claim limitation 1a of the current invention) and the protein capable of binding to ICAM-1 is a peptide capable of (the degree of binding is not specified) binding to a ligand (i.e. ICAM-1) (compare claim limitation 1b of the current invention). Therefore, Faanes teach the limitations of claim 1 of the current invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1,5,7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rieu et al. (as cited in IDS, J Cell Bio 1994;127:2081-2091) and Liu et al. (US 5,340,800).

Rieu et al. teach the peptide called A6 (figure 6) of sequence TGIRKVVRELFNITNGARKN which is identical to SEQ ID NO:126 of the current invention (compare claims 1,8 of the current invention). This particular peptide is from the A-domain of β2 integrin CR3 (CD11b/CD18) (title and page 2086) (compare claims 5,7 of the current invention) and used to identify binding of the hookworm-derived neutrophil adhesion inhibitor (NIF) (page 2086). Rieu teach that A6 (TGIRKVVRELFNITNGARKN) comprises the binding site for NIF (page 2089 first full paragraph). Rieu teach that the A-domain is a specific target for therapeutics and may be useful for treating hookworm.

Rieu does not specifically teach the A6 peptide (TGIRKVVRELFNITNGARKN) conjugated to a hydrophilic polymer.

Liu also teach peptides of beta subunits of integrin, specifically of CD18 (abstract, column 5-6). Liu teach that for convenience of administration that the peptides may be

augmented by derivitization, for example with polyethylene glycol (column 5 lines 53-66). Since Rieu teach the peptides as therapeutics one would be motivated to use the conjugation strategy as described by Liu for convenience of administration. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

It has been recently held that "Neither §103's enactment nor *Graham*'s analysis disturbed the Court's earlier instructions concerning the need for caution in granting a patent based on the combination of elements found in the prior art." KSR v. Teleflex, 550 U.S. ___, 82 USPQ2d 1385, 1389 (2007). The KSR court stated that "a combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." KSR at 1389. In the instant case, all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods and the combination would have yielded predictable results.

Furthermore, The KSR court concluded that "obvious to try" may be an appropriate test under 103. The Supreme Court stated in *KSR*

> When there is motivation
>
> > "to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, ___, 82 USPQ2d 1385, 1397 (2007).

In the instant case all the claimed elements (peptide of SEQ ID NO:126, integrin PEG conjugates) were known in the art as discussed above and one skilled in the art could have combined the elements by known methods and the combination would have yielded predictable

results. Since Rieu teach that the peptide A6 (TGIRKVVRELFNITNGARKN) comprises the binding site for NIF (page 2089 first full paragraph) and that the A-domain is a specific target for therapeutics and may be useful for treating hookworm one would be motivated to use the A6 peptide as a therapeutic. Since Liu teach that peptides (specifically integrins) may be derivitized for example with PEG for convenience of administration (column 5 lines 53-66) one would be motivated to conjugate peptide A6 with PEG. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1,5,7-8 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of copending Application No. 11/244,536 ('536) in view of Rieu et al. (as cited in IDS) and Liu et al. (US 5,340,800).

Claim 1 of copending Application No. 11/244,536 teach a composition comprising a selectin binding molecule linked to a hydrophilic polymer. Since the selectin binding molecule is identified in claim 7 (see table 1) as being an integrin (i.e. a peptide) the limitations of claims 1,5 of the current invention are met.

'536 does not expressly teach the elected species of the instant invention.

As stated above, Rieu et al. teach the peptide called A6 (figure 6) of sequence TGIRKVVRELFNITNGARKN which is identical to SEQ ID NO:126 of claim 8 of the current invention. Liu also teach peptides of beta subunits of integrin, specifically of CD18 (abstract, column 5-6). Liu teach that for convenience of administration that the peptides may be augmented by derivitization, for example with polyethylene glycol (column 5 lines 53-66). Since '536 teach binding molecules linked to hydrophilic polymers such as integrins (claim 7) one would be motivated to use the specific integrin peptide described by Rieu et al. and the specific polymer described by Liu et al. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

This is a provisional obviousness-type double patenting rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ronald T. Niebauer whose telephone number is 571-270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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PRIMARY EXAMINER

1/4/08

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